CLAIMS

We claim:

1. A method of classifying a tumor comprising the steps of:

providing a tumor sample;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the sample; and

classifying the tumor as belonging to a tumor subclass based on the results of the detecting step.

2. A method of classifying a tumor comprising the steps of:

providing a tumor sample;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the sample; and

classifying the tumor as belonging to a tumor subclass based on the results of the detecting step.

3. A method of classifying a tumor comprising the steps of:

providing a tumor sample;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the sample; and

classifying the tumor as belonging to a tumor subclass based on the results of the detecting step.

4. A method of classifying a tumor comprising the steps of:

providing a tumor sample;

detecting expression or activity of at least two genes selected from the group consisting of: a gene encoding the polypeptide of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the sample; and

classifying the tumor as belonging to a tumor subclass based on the results of the detecting step.

5. The method of any of claims 1, 2, 3, or 4, wherein the detecting step comprises detecting the polypeptide or polypeptides.

6. The method of claim 5, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6a. The method of claim 5, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6b. The method of claim 5, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6c. The method of claim 5, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

7. The method of any of claims 1, 2, 3, or 4, wherein classifying a tumor comprises:

stratifying a subject having the tumor for a clinical trial.

8. The method of claim 7, wherein the tumor is a breast tumor.

9. The method of any of claims 1, 2, 3, or 4, wherein the tumor is a breast tumor and the tumor subclass is a basal tumor subclass.

1a. The method of claim 1, further comprising:

providing diagnostic, prognostic, or predictive information based on the classifying step.

2a. The method of claim 2, further comprising:

providing diagnostic, prognostic, or predictive information based on the classifying step.

3a. The method of claim 3, further comprising:

providing diagnostic, prognostic, or predictive information based on the classifying step.

4a. The method of claim 4, further comprising:

providing diagnostic, prognostic, or predictive information based on the classifying step.

5a. The method of claim 5, further comprising:

providing diagnostic, prognostic, or predictive information based on the classifying step.

6aa. The method of claim 5a, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6ab. The method of claim 5a, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6ac. The method of claim 5a, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6ad. The method of claim 5a, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

9a. The method of any of claims 1a, 2a, 3a, or 4a, wherein the tumor is a breast tumor and the tumor subclass is a basal tumor subclass.

1g. The method of claim 1, further comprising:

selecting a treatment based on the classifying step.

2g. The method of claim 2, further comprising:

selecting a treatment based on the classifying step.

3g. The method of claim 3, further comprising:

selecting a treatment based on the classifying step.

4g. The method of claim 4, further comprising:

selecting a treatment based on the classifying step.

5g. The method of claim 5, further comprising:

selecting a treatment based on the classifying step.

6ag. The method of claim 5g, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6bg. The method of claim 5g, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6cg. The method of claim 5g, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6dg. The method of claim 5g, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

9g. The method of any of claims 1g, 2g, 3g, or 4g, wherein the tumor is a breast tumor and the tumor subclass is a basal tumor subclass.

1m. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the sample; and

providing diagnostic, prognostic, or predictive information based on the detecting step.

2m. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the sample; and

providing diagnostic, prognostic, or predictive information based on the detecting step.

3m. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the sample; and

providing diagnostic, prognostic, or predictive information based on the detecting step.

4m. A method of testing a subject comprising the steps of:

providing a sample isolated from the subject;

detecting expression or activity of at least two genes selected from the group consisting of: a gene encoding the polypeptide of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the sample; and

providing diagnostic, prognostic, or predictive information based on the detecting step.

5m. The method of any of claims 1m, 2m, 3m, or 4m, wherein the detecting step comprises detecting the polypeptide or polypeptides.

6m. The method of claim 5m, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6ma. The method of claim 5m, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6mb. The method of claim 5m, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6mc. The method of claim 5m, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

9m. The method of any of claims 1m, 2m, 3m, or 4m, wherein the sample is selected from the group consisting of:

a blood sample, a urine sample, a serum sample, an ascites sample, a saliva sample, a cell, and a portion of tissue.

10m. The method of any of claims 1m, 2m, 3m, or 4m, wherein the sample is a tumor sample.

11m. The method of claim 10m, wherein the tumor sample is a breast tumor sample.

1r. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the sample; and

stratifying the subject for a clinical trial based on the detecting step.

2r. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the sample; and

stratifying the subject for a clinical trial based on the detecting step.

3r. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the sample; and

stratifying the subject for a clinical trial based on the detecting step.

4r. A method of testing a subject comprising the steps of:

providing a sample isolated from the subject;

detecting expression or activity of at least two genes selected from the group consisting of: a gene encoding the polypeptide of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the sample; and

stratifying the subject for a clinical trial based on the detecting step.

5r. The method of any of claims 1r, 2r, 3r, or 4r, wherein the detecting step comprises detecting the polypeptide or polypeptides.

6r. The method of claim 5r, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6ra. The method of claim 5r, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6rb. The method of claim 5r, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6rc. The method of claim 5r, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

9r. The method of any of claims 1r, 2r, 3r, or 4r, wherein the sample is selected from the group consisting of:

a blood sample, a urine sample, a serum sample, an ascites sample, a saliva sample, a cell, and a portion of tissue.

10r. The method of any of claims 1r, 2r, 3r, or 4r, wherein the sample is a tumor sample.

11r. The method of claim 10r, wherein the tumor sample is a breast tumor sample.

1q. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the sample; and

selecting a treatment based on the detecting step.

2q. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the sample; and

selecting a treatment based on the detecting step.

3q. A method of testing a subject comprising the steps of:

providing a sample isolated from a subject;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the sample; and

selecting a treatment based on the detecting step.

4q. A method of testing a subject comprising the steps of:

providing a sample isolated from the subject;

detecting expression or activity of at least two genes selected from the group consisting of: a gene encoding the polypeptide of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the sample; and

selecting a treatment based on the detecting step.

5q. The method of any of claims 1q, 2q, 3q, or 4q, wherein the detecting step comprises detecting the polypeptide or polypeptides.

6q. The method of claim 5q, wherein the polypeptide is detected by performing immunohistochemical analysis on the sample using an antibody that specifically binds to the polypeptide.

6qa. The method of claim 5q, wherein the polypeptide is detected by performing an ELISA assay using an antibody that specifically binds to the polypeptide.

6qb. The method of claim 5q, wherein the polypeptide is detected using an antibody array comprising an antibody that specifically binds to the polypeptide.

6qc. The method of claim 5q, wherein the detecting step comprises:

detecting modification of a substrate by the polypeptide.

9q. The method of any of claims 1q, 2q, 3q, or 4q, wherein the sample is selected from the group consisting of:

a blood sample, a urine sample, a serum sample, an ascites sample, a saliva sample, a cell, and a portion of tissue.

10m. The method of any of claims 1m, 2m, 3m, or 4m, wherein the sample is a tumor sample.

11m. The method of claim 10m, wherein the tumor sample is a breast tumor sample.

20. An antibody that specifically binds to an epitope found in a polypeptide whose amino acid sequence the amino acid sequence of SEQ ID NO:1, and wherein the antibody recognizes basal cells in normal mammary lactation glands.

21. The antibody of claim 21, wherein the antibody distinguishes basal cells from luminal cells in normal mammary lactation glands.

22. The antibody of claim 20, wherein the antibody is a monoclonal antibody.

23. The antibody of claim 20, wherein the antibody is a polyclonal antibody.

24. The antibody of claim 20, wherein the antibody recognizes an epitope found in a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6.

25. An antibody that specifically binds to an epitope found in a polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:2, and wherein the antibody recognizes basal cells in normal mammary lactation glands.

26. The antibody of claim 25, wherein the antibody distinguishes basal cells from luminal cells in normal mammary lactation glands.

27. The antibody of claim 25, wherein the antibody is a monoclonal antibody.

28. The antibody of claim 25, wherein the antibody is a polyclonal antibody.

29. The antibody of claim 25, wherein the antibody recognizes an epitope found in a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.

30. An antibody that specifically binds to an epitope found in a polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:3, and wherein the antibody recognizes basal cells in normal mammary lactation glands.

31. The antibody of claim 30, wherein the antibody distinguishes basal cells from luminal cells in normal mammary lactation glands.

32. The antibody of claim 30, wherein the antibody is a monoclonal antibody.

33. The antibody of claim 30, wherein the antibody is a polyclonal antibody.

34. The antibody of claim 30, wherein the antibody recognizes an epitope found in a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12.

38. A kit for tumor diagnosis comprising:

one or more of the antibodies of any of claims 20 through 34;

instructions for use of the kit; and

a control slide comprising breast tissue samples for testing reagents in the kit.

40. A method of testing a compound or a combination of compounds for activity against tumors comprising steps of:

obtaining or providing tumor samples taken from subjects who have been treated with the compound or combination of compounds, wherein the tumors fall within a tumor subclass;

comparing the response rate of tumors that fall within the tumor subclass and have been treated with the compound with the overall response rate of tumors that have been treated with the compound or combination of compounds or with the response rate of tumors that do not fall within the subclass and have been treated with the compound or combination of compounds; and

identifying the compound or combination of compounds as having selective activity against tumors in the tumor subclass if the response rate of tumors in the subclass is greater than the overall response rate or the response rate of tumors that do not fall within the subclass.

41. The method of claim 40, wherein the tumors are breast tumors.

42. The method of claim 41, wherein the tumor subclass is a basal tumor subclass.

43. The method of claim 41, wherein the tumors are classified according to the method of any of claims 1, 2, 3, or 4.

44. The method of claim 41, wherein the tumor subclass is a basal tumor subclass and wherein a tumor is identified as belonging to the tumor subclass based on evidence of expression of one or more basal marker genes in the sample.

45. The method of claim 44, wherein evidence of expression comprises presence of a protein encoded by a basal marker gene, and wherein the evidence of expression is obtained using an antibody that binds to the protein.

46. The method of claim 45, wherein the basal marker gene encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:1.

47. The method of claim 45, wherein the basal marker gene encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

48. The method of claim 45, wherein the basal marker gene encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:3.

49. The method of claim 40, wherein the samples are present within a tissue array.

60. A method of testing a compound or a combination of compounds for activity against tumors comprising steps of:

treating subjects in need of treatment for tumors with the compound or combination of compounds;

comparing the response rate of tumors that fall within a tumor subclass with the overall response rate of tumors or with the response rate of tumors that do not fall within the subclass; and

identifying the compound or combination of compounds as having selective activity against tumors in the tumor subclass if the response rate of tumors in the subclass is greater than the overall response rate or the response rate of tumors that do not fall within the subclass.

61. The method of claim 60, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

determining whether the tumors fall within a tumor subclass; and

stratifying the subjects based on the results of the determining step prior to performing the treating step.

62. The method of claim 60, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the the treating step.

63. The method of claim 60, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

64. The method of claim 60, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

65. The method of claim 60, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of at least two genes, wherein each of the genes encodes a polypeptide whose sequence comprises a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

80. A method of testing a compound or a combination of compounds for activity against tumors comprising steps of:

treating subjects in need of treatment for tumors with the compound or combination of compounds or with an alternate compound, wherein the tumors fall within a tumor subclass;

comparing the response rate of tumors treated with the compound or combination of compounds with the response rate of tumors treated with the alternate compound; and

identifying the compound or combination of compounds as having superior activity against tumors in the tumor subclass, as compared with the alternate compound, if the response rate of tumors treated with the compound or combination of compounds is greater than the response rate of tumors treated with the alternate compound.

81. The method of claim 80, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

determining whether the tumors fall within a tumor subclass; and

stratifying the subjects based on the results of the determining step prior to performing the treating step.

82. The method of claim 80, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:1 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

83. The method of claim 80, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:2 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

84. The method of claim 80, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

85. The method of claim 80, further comprising the steps of:

providing tumor samples from subjects in need of treatment for tumors;

detecting expression or activity of at least two genes, wherein each of the genes encodes a polypeptide whose sequence comprises a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 in the samples; and

stratifying the subjects based on the results of the detecting step prior to performing the treating step.

86. The method of any of claims 80, 81, 82, 83, 84, or 85, wherein the alternate compound is a compound approved by the U.S. Food and Drug administration for treatment of tumors.

100. A method of treating a subject comprising steps of:

identifying a subject as having a tumor in a basal tumor subclass; and

administering a compound identified according to the method of any of claims 40, 41, 42, or 45 to the subject.

101. A method of treating a subject comprising steps of:

identifying a subject as having a tumor in a basal tumor subclass; and

administering a compound identified according to the method of any of claims 60, 61, 62, 63, 64, or 65 to the subject.

103. A method of treating a subject comprising steps of:

identifying a subject as having a tumor in a basal tumor subclass; and

administering a compound identified according to the method of any of claims 80, 81, 82, 83, 84, or 85 to the subject.

120. A method of treating a subject comprising steps of:

providing a subject in need of treatment for cancer;

administering to the subject an antibody that specifically binds to a polypeptide having an amino acid sequence comprising the sequence of SEQ ID NO:1.

121. A method of treating a subject comprising steps of:

providing a subject in need of treatment for a tumor;

administering to the subject an antibody that specifically binds to a polypeptide having an amino acid sequence comprising the sequence of SEQ ID NO:2.

122. A method of treating a subject comprising steps of:

providing a subject in need of treatment for a tumor;

administering to the subject an antibody that specifically binds to a polypeptide having an amino acid sequence comprising the sequence of SEQ ID NO:3.

130. The method of any of claims 120, 121, or 122, wherein the tumor is a breast tumor, and wherein the method further comprises the step of:

identifying the tumor as belonging to a basal tumor subclass.

131. The method of any of claims 120, 121, or 122, wherein the antibody is conjugated with a toxic molecule.

140. A method of treating a subject comprising steps of:

providing a subject in need of treatment for cancer;

administering to the subject a compound that activates or inhibits a gene that encodes an amino acid having a sequence comprising the sequence of SEQ ID NO:1, or that activates or inhibits an expression product of the gene.

141. A method of treating a subject comprising steps of:

providing a subject in need of treatment for a tumor;

administering to the subject a compound that activates or inhibits a gene that encodes an amino acid having a sequence comprising the sequence of SEQ ID NO:2, or that activates or inhibits an expression product of the gene.

142. A method of treating a subject comprising steps of:

providing a subject in need of treatment for a tumor;

administering to the subject a compound that activates or inhibits a gene that encodes an amino acid having a sequence comprising the sequence of SEQ ID NO:3, or that activates or inhibits an expression product of the gene.

150. A composition comprising:

two or more compounds identified according to the method of any of claims 40, 60, or 80.

151. A pharmaceutical composition comprising:

the composition of claim 150; and

a pharmaceutically acceptable carrier.

160. A composition comprising:

a compound identified according to the method of any of claims 40, 60, or 80;

a second compound, wherein the second compound is approved by the U.S. Food and Drug administration for the treatment of cancer or has shown potential efficacy against cancer in pre-clinical studies.

161. A pharmaceutical composition comprising:

the composition of claim 160; and

a pharmaceutically acceptable carrier.